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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,068	04/14/2004	Chih-Ping Liu	55600-8014.US03	7994
22918	7590	04/24/2006	EXAMINER	
PERKINS COIE LLP P.O. BOX 2168 MENLO PARK, CA 94026			HISSONG, BRUCE D	
			ART UNIT	PAPER NUMBER

1646

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/825,068

Applicant(s)

LIU ET AL.

Examiner

Bruce D. Hissong, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 August 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 5/5/2004.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. The preliminary amendment filed 8/2/2004 has been entered into the record.
2. The preliminary amendment filed 5/5/2004 has been entered into the record.
3. Claims 1-14 are currently pending and are the subject of this office action.

Priority

1. The instant application was filed on 4/14/2004, and claims benefit of provisional application 60/552279, filed on 3/10/2004. The instant application is also a continuation-in-part of application 09/910,406 (now US 6,982,081), filed on 7/19/2001, which claims benefit to provisional application 60/219,128, filed on 7/19/2000.

The later-filed application must be an application for a patent for an invention that is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosures of the prior-filed applications, Application Nos. 09/910,406 and 60/219,128, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. In the instant case, Application Nos. 09/910,406 and 60/219,128 do not provide enablement or support for the claims of the instant application which are drawn to methods of increasing the IL-10/IL-12 blood ratio by administering interferon (IFN)- τ to produce an increase in blood IL-10 levels. Although the Application Nos. 09/910,406 and 60/219,128 disclose oral administration of IFN- τ , there is no teaching or disclosure of modulation of IL-10 levels, or increasing the blood IL-10/IL-12 ratio in subjects who received orally administered IFN- τ . Thus, Applications 09/910,406 and 60/219,128 clearly do not contemplate methods of increasing the blood IL-10/IL-12 ratios, and therefore are not enabling for the claims of the instant application.

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2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on 10/17/2000. It is noted, however, that applicant has not filed a certified copy of the JP 317160 application as required by 35 U.S.C. 119(b). However, if Applicants do file a Certified English translation, and the subject matter fully supports and enables the claims of the instant application, the priority date will be reconsidered.

3. Therefore, the earliest effective filing date of the instant application has been determined to be 3/10/2004, which is the filing date of provisional application 60/552279.

Information Disclosure Statement

The information disclosure statement received on 5/5/2004 has been fully considered by the Examiner.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is a conclusion step for the method of increasing the IL-10/IL-12 blood ratio in a subject. Claim 1 recites a conclusion step of assessing a clinical endpoint in a subject, rather than a conclusion step that assesses the IL-10/IL-12 blood ratio and thus relates to the preamble of the claim.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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1. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of increasing the IL-10/IL-12 blood ratio comprising orally administering IFN- τ defined by SEQ ID NOs 2 and 3, does not reasonably provide enablement for methods of increasing the blood IL-10/IL-12 ratio by orally administering any other IFN- τ . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of claims. *Ex Parte Forman*, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The specification, on page 7, paragraph 0036, states that IFN- τ can refer to a family of interferon proteins having about 45 to 68% amino acid homology with α -interferons and greater than 70% amino acid homology to known IFN- τ sequences. The specification, on page 8, paragraph 0037, also teaches that an ovine IFN- τ protein is one having about 80%, more preferably 90%, sequence homology to the sequence identified by SEQ ID NO: 2. Thus, the breadth of the claims is excessive because the claims read on methods of administering any protein with 70% or greater homology to known IFN- τ sequences, including molecules with at least 80% homology to the protein of SEQ ID NO: 2, and also including any ovine or bovine IFN- τ polypeptide. There is no guidance or examples in the specification that teach that any IFN- τ with less than 100% homology to SEQ ID NO: 2 or 3 can be orally administered to a subject, resulting in an increase in the IL-10/IL-12 blood ratio. A person of ordinary skill in the art would not be able to predict which of the many possible polypeptide sequences with less than 100% homology to SEQ ID NO: 2 or 3 would be able to increase the IL-10/IL-12 blood ratio, and thus be used commensurate in scope with the claims.

In summary, due to the excessive breadth of the claims, which read on a method of administering any IFN- τ polypeptide, peptide, or fragment thereof, the lack of guidance or examples in the specification which teaches administration of any polypeptide with less than 100% homology to SEQ ID NO: 2 or 3, and unpredictability in the art regarding the effects of such polypeptides, a person of ordinary skill in the art would require further, undue

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experimentation to make and use any IFN- τ polypeptide, other than those of SEQ ID NO: 2 or 3, in a method of increasing the IL-10/IL-12 blood ratio in subject.

2. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing the IL-10/IL-12 ratio in a subject suffering from an autoimmune disorder, or a method for inhibiting progression of an autoimmune disorder, wherein the disorder is multiple sclerosis, does not reasonably provide enablement for inhibiting disease progression or increasing the IL-10/IL-12 ratio in a subject suffering from any other autoimmune disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The breadth of the claims is excessive because the claims read on any autoimmune disorder. While the specification provides guidance and examples showing orally administered IFN- τ of SEQ ID NO:3 results in an increase in the IL-10/IL-12 blood ratio in multiple sclerosis patients, and teaches that oral administration of the protein of SEQ ID NO: 3 is effective in treating multiple sclerosis, there is no guidance or examples that teach that any other autoimmune disease can be treated with the polypeptide of SEQ ID NO: 3 or any other IFN- τ polypeptide. A person of ordinary skill in the art would know that autoimmune disorders encompass a wide range of diseases, both organ-specific and systemic, whose etiologies and pathogenesis are not fully known but are understood to be influenced by multiple factors, including genetic and environmental influences (see specification, paragraphs 0106-0108). Thus, the skilled artisan would not be able to predict which of the many possible autoimmune disorders would respond favorably to increasing the IL-10/IL-12 blood ratio by oral administration of IFN- τ . For example, would type I autoimmune/hypersensitivity reactions, which are known to be associated with Th2 responses, be treatable by a method to increase the IL-10/IL-12 ratio? For these reasons, it would require further, undue experimentation on the part of a person of ordinary skill in the art to determine which autoimmune disease could be treated by orally administered IFN- τ . Finally, claims 8-14 do not specify a population of individuals to be treated. Claim 8 recites inhibiting autoimmune disease progression in a subject, and given the broadest reasonable interpretation, could read on preventing disease progression in a person with autoimmune disease, and could also read on preventing disease progression in a healthy individual. The specification does not provide guidance or examples showing that the administration of any IFN- τ polypeptide could be used to

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prevent any autoimmune disease in a healthy subject, and therefore a person of ordinary skill in the art would not know how to make and use any IFN- τ polypeptide to prevent autoimmune disease in a healthy individual.

In summary, due to the excessive breadth of the claims, which read on methods for treating or increasing the IL-10/IL-12 ratio in a subject suffering from any autoimmune disease by orally administering IFN- τ , the lack of guidance and examples in the specification showing that any disease other than multiple sclerosis can be treated by orally administered IFN- τ , and the unpredictability inherent in the invention regarding which diseases can be treated, a person of ordinary skill in the art would require further, undue experimentation to determine which autoimmune diseases will favorably respond to an orally administered IFN- τ -stimulated increase in the IL-10/IL-12 blood ratio.

Claim Rejections - 35 USC § 112, first paragraph – written description

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to oral administration of IFN- τ polypeptides. As discussed in the above 35 U.S.C. 112, first paragraph enablement rejection #1, the specification states that IFN- τ proteins can include any ovine or bovine IFN- τ protein, or any protein with at least 70% homology to a known IFN- τ protein, or at least 80% homology to the proteins of SEQ ID NO: 2 or 3. The claims do not require the IFN- τ of the instant invention to have any particular structure other than to have at least 70% amino acid homology to any IFN- τ polypeptide. The specification does not teach what deletions, additions, or substitutions can be made in an IFN- τ polypeptide, resulting in a protein that is at least 70% homology to any known IFN- τ protein, and there is no disclosure of any particular region of any IFN- τ polypeptide, from any species, that must be conserved in order to maintain the desired biological function. Thus, the Applicants have not fully described the genus of IFN- τ polypeptides capable of increasing the blood IL-10/IL-12 ratio, and thus capable of being used commensurate in scope with the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus.

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The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a requirement that the IFN- τ proteins have at least 70% homology to any known IFN- τ protein. There is no identification of any particular portion of an IFN- τ polypeptide that must be conserved in order to maintain the desired biological activity (i.e. the ability to increase the IL-10/IL-12 blood ratio). Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1. Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soos *et al* (WO 97/3607 – cited in the information disclosure statement received on 5/5/2004), in view of van Boxel-Dezaire *et al* (*Ann. Neurol.*, 1999, Vol. 45, p. 695-703 – cited in information disclosure statement received on 5/5/2004), and further in view of Petereit *et al* (*J. Neurol. Sci.*, 2003, Vol. 206, p. 209-214 – cited in information disclosure statement received on 5/5/2004). The claims of the instant invention are drawn to methods of increasing the IL-10/IL-12 blood ratio, or methods of inhibiting the progression of autoimmune disease, by oral administration of IFN- τ polypeptides. Soos *et al* teach oral administration of IFN- τ polypeptides for the treatment of multiple sclerosis (see abstract; p. 5, lines 8-21; p. 11, line 5 – p. 12, line 16, p. 23, Example 1; and all claims). Specifically, Soos *et al* teaches administration of IFN- τ defined by SEQ ID NO: 2, which exhibits 100% homology to the polypeptide defined by SEQ ID NO: 2 of the instant application (see sequence comparison 1). Soos *et al* also teaches that other autoimmune disorders, including type I diabetes mellitus, lupus erythematosus, Crohn's disease, rheumatoid arthritis, and psoriasis, can also be treated by orally administered IFN- τ (p. 11, lines 17-21), and also teaches that orally administered IFN- τ increases serum IL-10 levels (p. 26, Example 5).

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Soos *et al* is silent regarding oral administration of IFN- τ at doses of at least 5×10^8 units/day, and does not teach increasing the IL-10/IL-12 blood ratio.

van Boxel-Dezaire *et al* teaches that multiple sclerosis is characterized by decreased IL-10 levels and increased IL-12p40 levels (see Figures 1-3), and suggests that IL-10 plays an important role in the control of disease progression. Petereit *et al* teach that multiple sclerosis patients with higher IL-10 secretion had higher clinical disability scores than patients with lower IL-10 secretion (see abstract and p. 211-212).

Therefore, it would have been obvious to a person of ordinary skill in the art, at the time the instant invention was made, to combine the teachings of Soos *et al* with those of van Boxel-Dezaire *et al* and Petereit *et al* to orally administer IFN- τ to increase the IL-10/IL-12 blood ratio in order to treat autoimmune disease such as multiple sclerosis. Soos *et al* provides the motivation to treat multiple sclerosis, and other autoimmune disorders, with orally administered IFN- τ . Petereit *et al* and van Boxel-Dezaire *et al* provide the motivation to increase the production of IL-10, and to increase the IL-10/IL-12 ratio in multiple sclerosis. Furthermore, by teaching that IL-10 secretion is increased after oral IFN-t administration, Soos *et al* provides further motivation to use orally administered IFN-t, and also provides a reasonable expectation of success by insuring that the IL-10 levels, and therefore IL-10/IL-12 ratios, would increased in the treated patients.

Although Soos *et al* does not specifically teach oral administration of IFN- τ at doses of at least 5×10^8 units/day, a person of ordinary skill in the art would be motivated to optimize the dosage required for effective treatment. Furthermore, because Soos *et al* teaches that IFN- τ treatment is not associated with the toxicity associated with administration of other IFNs (p. 12, line 26 – p. 13, line 4), the skilled artisan would be assured that the dosage optimization would likely not harm the patient. Additionally, while Soos *et al* does not specifically teach administration to the intestinal tract of a subject, such methods are well-known in the art and would be within the skilled artisan's abilities. Finally, Soos *et al* teaches that cessation of oral IFN-t administration results in a relapse of clinical symptoms (p. 26, Example 6), providing the motivation for the skilled artisan to continue administration during the period the patient exhibits symptoms until the desired clinical endpoint, a reduction in symptoms, is reached.

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Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the following claims in the indicated applications:

<u>Application No.</u>	<u>Claims</u>
10/825382	1-15
10/825457	1-6
10/824710	1-4, 16-17
11/040706	1-6, 25
10/884741	1-4, 8-10, 19-22
11/112369	1, 17, 18
10/991653	1, 5-11
10/719472	1-4
10/346269	1-5

Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflicting claims of the applications cited above are drawn to methods of oral administration of IFN- τ . The claims of the instant application do not identify a population

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for treatment, and thus the claims read on administration of IFN- τ to all possible subjects. Although the conflicting claims are not identical, they are not patentably distinct from each other because the process steps of orally administering IFN- τ in the same dosage as specified in the instant application, are the same regardless of whether the purpose is to stimulate IL-10 production, or treat Hepatitis C infections, or stimulate any other biological activity (Ex parte Novitski, 26 USPQ 1391). The instant method steps of oral administration of IFN- τ would inherently perform these activities, and because a specific population in need of treatment is not defined in claims of the instant application, the instant method steps would encompass any population claimed in the conflicting applications.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hisson, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BDH
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ROBERT S. LANDSMAN, PH.D.
PRIMARY EXAMINER